```
* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *
  * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * *

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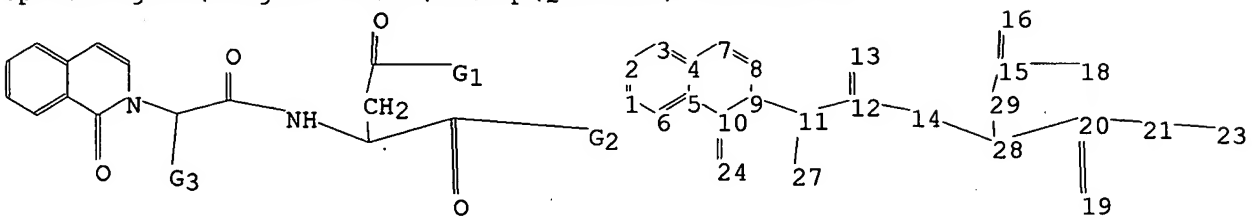


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chain nodes :
11  12  13  14  15  16  18  19  20  21  23  24  27  28  29
ring nodes :
1  2  3  4  5  6  7  8  9  10
chain bonds :
9-11  10-24  11-12  11-27  12-13  12-14  14-28  15-18  15-16  15-29  19-20  20-21
20-28  21-23  28-29
ring bonds :
1-2  1-6  2-3  3-4  4-5  4-7  5-6  5-10  7-8  8-9  9-10
exact/norm bonds :
4-7  5-10  7-8  8-9  9-10  9-11  10-24  11-27  12-13  12-14  14-28  15-18  15-16
19-20  21-23
exact bonds :
11-12  15-29  20-21  20-28  28-29
normalized bonds :
1-2  1-6  2-3  3-4  4-5  5-6
isolated ring systems :
containing 1 :


G1:O,N

G2:O,X

G3:Cy,Ak

Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
11:CLASS  12:CLASS  13:CLASS  14:CLASS  15:CLASS  16:CLASS  18:CLASS  19:CLASS
20:CLASS  21:CLASS  23:CLASS  24:CLASS  27:CLASS  28:CLASS  29:CLASS



L1      STRUCTURE UPLOADED

=> dis l1
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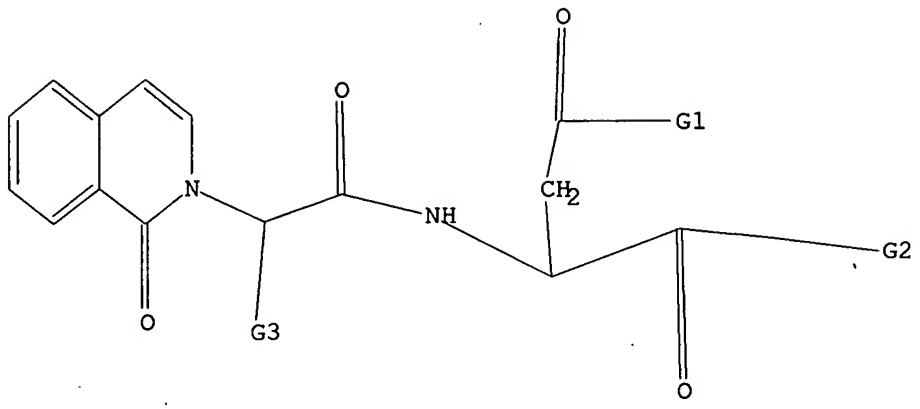
L1 HAS NO ANSWERS
L1 STR



G1 O,N
G2 O,X
G3 Cy,Ak

Structure attributes must be viewed using STN Express query preparation.

=> s l1 sam
L2 4 SEA SSS SAM L1

=> s l1 ful
L3 50 SEA SSS FUL L1

=> file caplus

FILE COVERS 1907 - 8 Jul 2005 VOL 143 ISS 3
FILE LAST UPDATED: 7 Jul 2005 (20050707/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3
L4 6 L3

=> s l4 and pd< december 2002
22523224 PD< DECEMBER 2002
(PD<20021200)
L5 1 L4 AND PD< DECEMBER 2002

=> s l4 not l5
L6 5 L4 NOT L5

=> dis l6 1-5 bib abs hitstr

L6 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:565214 CAPLUS
DN 141:106388

TI Preparation of 4-oxo-3-(1-oxo-1H-isoquinolin-2-ylacetylamino)-pentanoic acid ester and amide derivatives as caspase inhibitors

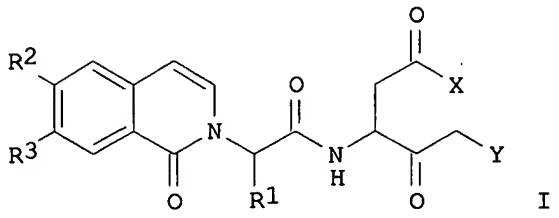
IN Charrier, Jean-Damien; Mortimore, Michael; Studley, John R.
PA Vertex Pharmaceuticals Incorporated, USA

SO PCT Int. Appl., 104 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004058718	A1	20040715	WO 2003-US40870	20031222
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004192612	A1	20040930	US 2003-743563	20031222
PRAI US 2002-435133P	P	20021220		

OS MARPAT 141:106388

GI



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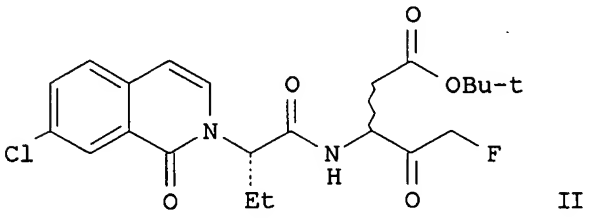


II

AB The title compds. of formula I [X = alkoxy, (substituted) NH2, etc.; Y = halo, trifluorophenoxy, tetrafluorophenoxy; R1 = alkyl; R2, R3 = H, halo, OCF3, CN, CF3] are prepared The present invention also provides pharmaceutical compns. and methods using such compns. for treating a caspase-mediated disease, particularly in the central nervous system. Thus, II was prepared from 7-chloroisochromen-1-one (preparation given), (S)-2-aminobutyric acid tert-Bu ester and 3-amino-5-fluoro-4-hydroxypentanoic acid tert-Bu ester.

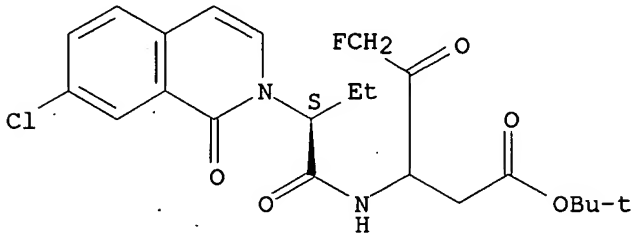
IT **640286-59-5P 721397-83-7P**

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of (oxoisoquinolinylacetylamino)-oxopentanoic acid ester and amide derivs. as caspase inhibitors)

RN 640286-59-5 CAPLUS

CN Pentanoic acid, 3-[[(2S)-2-(7-chloro-1-oxo-2(1H)-isoquinolinyl)-1-oxobutyl]amino]-5-fluoro-4-oxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

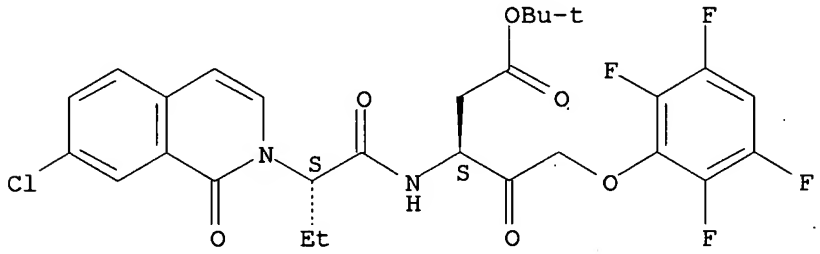
Absolute stereochemistry.



RN 721397-83-7 CAPLUS

CN Pentanoic acid, 3-[[(2S)-2-(7-chloro-1-oxo-2(1H)-isoquinolinyl)-1-oxobutyl]amino]-4-oxo-5-(2,3,5,6-tetrafluorophenoxy)-, 1,1-dimethylethyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



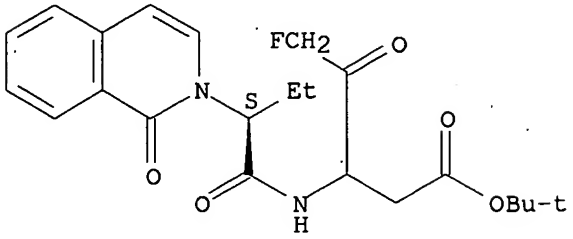
IT **721397-79-1P 721397-80-4P 721397-81-5P**
721397-82-6P 721397-84-8P 721397-85-9P
721397-86-0P 721397-87-1P 721397-88-2P
721397-89-3P 721397-90-6P 721397-91-7P
721397-92-8P 721397-93-9P 721397-94-0P
721397-95-1P 721397-96-2P 721397-97-3P
721397-98-4P 721397-99-5P 721398-00-1P
721398-01-2P 721398-02-3P 721398-03-4P
721398-04-5P 721398-05-6P 721398-06-7P
721398-07-8P 721398-08-9P 721398-09-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (oxoisoquinolinylacetylamino)-oxopentanoic acid ester and amide derivs. as caspase inhibitors)

RN 721397-79-1 CAPLUS

CN Pentanoic acid, 5-fluoro-4-oxo-3-[[(2S)-1-oxo-2-(1-oxo-2(1H)-isoquinolinyl)butyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX

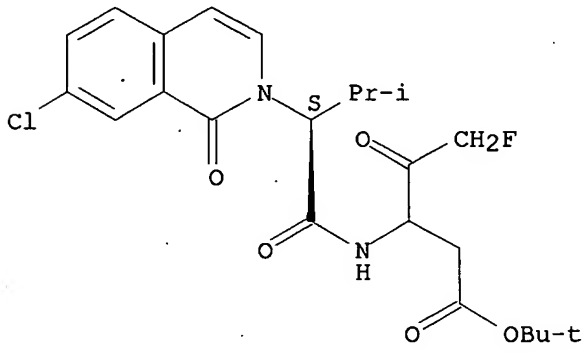
NAME)

Absolute stereochemistry.



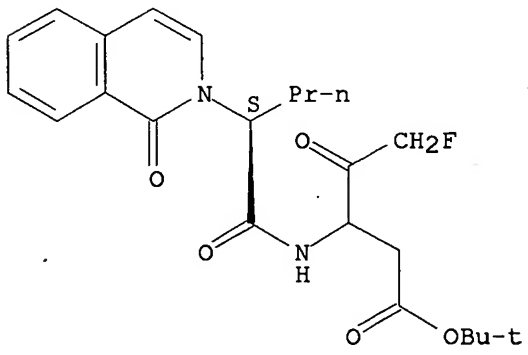
RN 721397-80-4 CAPLUS
CN Pentanoic acid, 3-[[(2S)-2-(7-chloro-1-oxo-2(1H)-isoquinolinyl)-3-methyl-1-oxobutyl]amino]-5-fluoro-4-oxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 721397-81-5 CAPLUS
CN Pentanoic acid, 5-fluoro-4-oxo-3-[[(2S)-1-oxo-2-(1-oxo-2(1H)-isoquinolinyl)pentyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

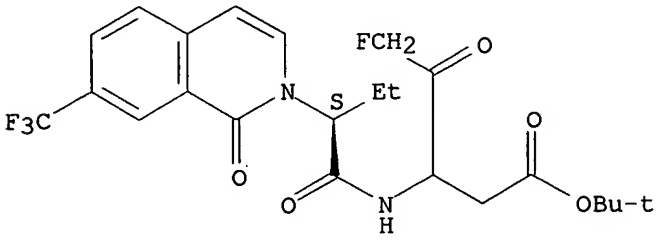
Absolute stereochemistry.



RN 721397-82-6 CAPLUS
CN Pentanoic acid, 5-fluoro-4-oxo-3-[[(2S)-1-oxo-2-[1-oxo-7-(trifluoromethyl)-

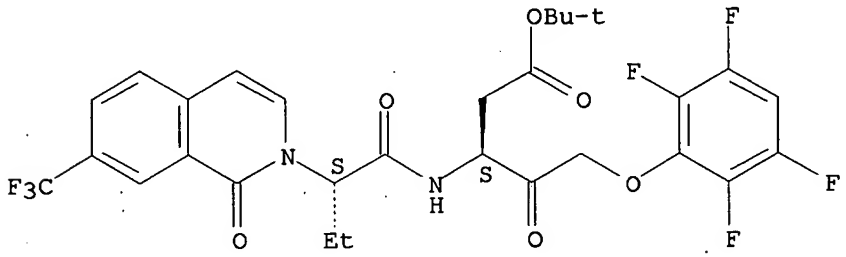
2(1H)-isoquinolinyl]butyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



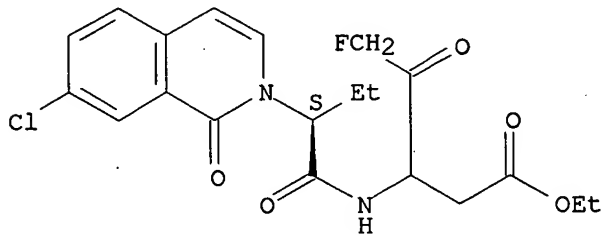
RN 721397-84-8 CAPLUS
CN Pentanoic acid, 4-oxo-3-[[(2S)-1-oxo-2-[1-oxo-7-(trifluoromethyl)-2(1H)-isoquinolinyl]butyl]amino]-5-(2,3,5,6-tetrafluorophenoxy)-, 1,1-dimethylethyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



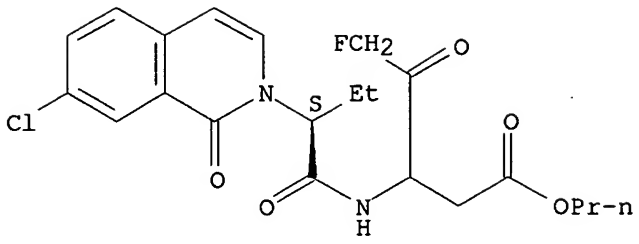
RN 721397-85-9 CAPLUS
CN Pentanoic acid, 3-[[(2S)-2-(7-chloro-1-oxo-2(1H)-isoquinolinyl)-1-oxobutyl]amino]-5-fluoro-4-oxo-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



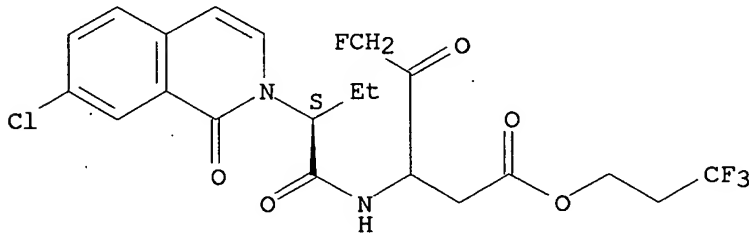
RN 721397-86-0 CAPLUS
CN Pentanoic acid, 3-[[(2S)-2-(7-chloro-1-oxo-2(1H)-isoquinolinyl)-1-oxobutyl]amino]-5-fluoro-4-oxo-, propyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



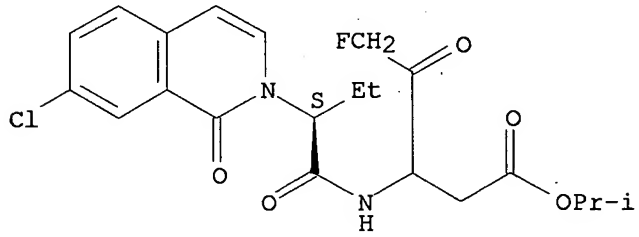
RN 721397-87-1 CAPLUS
CN Pentanoic acid, 3-[[(2S)-2-(7-chloro-1-oxo-2(1H)-isoquinolinyl)-1-oxobutyl]amino]-5-fluoro-4-oxo-, 3,3,3-trifluoropropyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



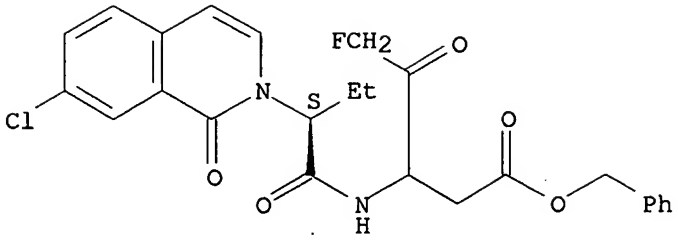
RN 721397-88-2 CAPLUS
CN Pentanoic acid, 3-[[(2S)-2-(7-chloro-1-oxo-2(1H)-isoquinolinyl)-1-oxobutyl]amino]-5-fluoro-4-oxo-, 1-methylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



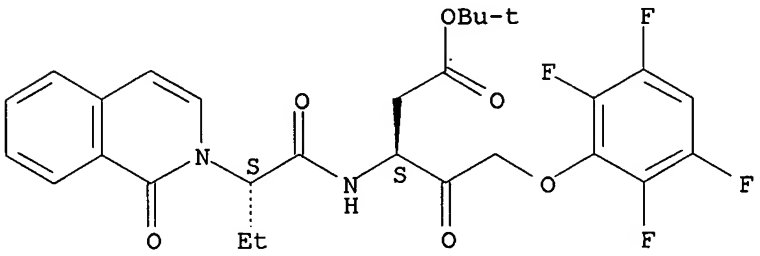
RN 721397-89-3 CAPLUS
CN Pentanoic acid, 3-[[(2S)-2-(7-chloro-1-oxo-2(1H)-isoquinolinyl)-1-oxobutyl]amino]-5-fluoro-4-oxo-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



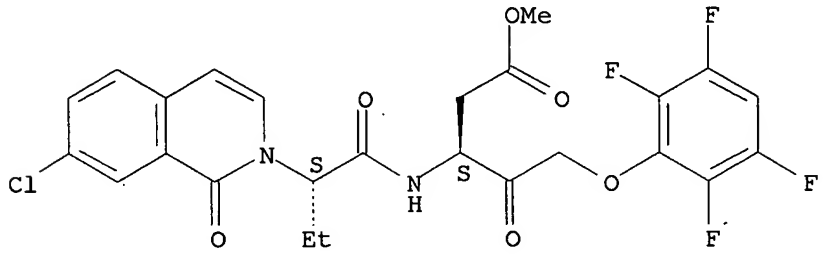
RN 721397-90-6 CAPLUS
CN Pentanoic acid, 4-oxo-3-[[(2S)-1-oxo-2-(1-oxo-2(1H)-isoquinolinyl)butyl]amino]-5-(2,3,5,6-tetrafluorophenoxy)-, 1,1-dimethylethyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



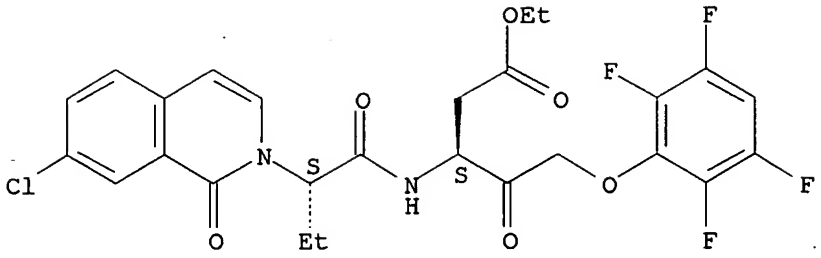
RN 721397-91-7 CAPLUS
CN Pentanoic acid, 3-[[(2S)-2-(7-chloro-1-oxo-2(1H)-isoquinolinyl)-1-oxobutyl]amino]-4-oxo-5-(2,3,5,6-tetrafluorophenoxy)-, methyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



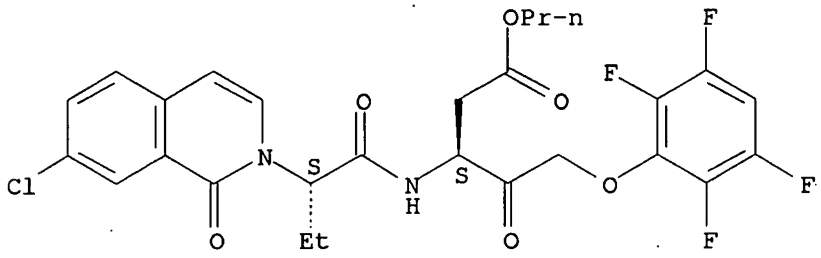
RN 721397-92-8 CAPLUS
CN Pentanoic acid, 3-[[(2S)-2-(7-chloro-1-oxo-2(1H)-isoquinolinyl)-1-oxobutyl]amino]-4-oxo-5-(2,3,5,6-tetrafluorophenoxy)-, ethyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



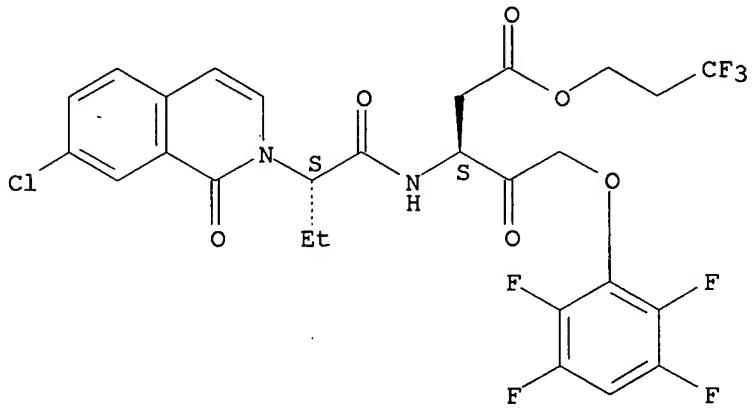
RN 721397-93-9 CAPLUS
CN Pentanoic acid, 3-[[(2S)-2-(7-chloro-1-oxo-2(1H)-isoquinolinyl)-1-oxobutyl]amino]-4-oxo-5-(2,3,5,6-tetrafluorophenoxy)-, propyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



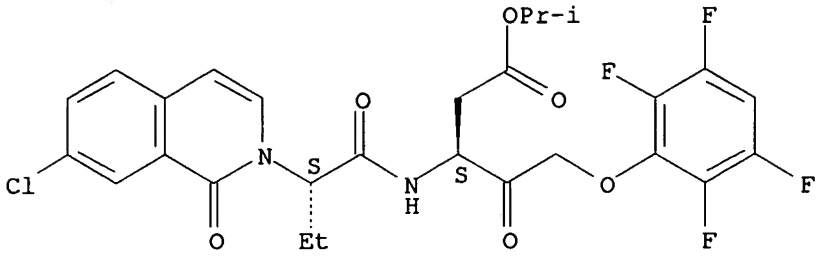
RN 721397-94-0 CAPLUS
CN Pentanoic acid, 3-[[(2S)-2-(7-chloro-1-oxo-2(1H)-isoquinolinyl)-1-oxobutyl]amino]-4-oxo-5-(2,3,5,6-tetrafluorophenoxy)-, 3,3,3-trifluoropropyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



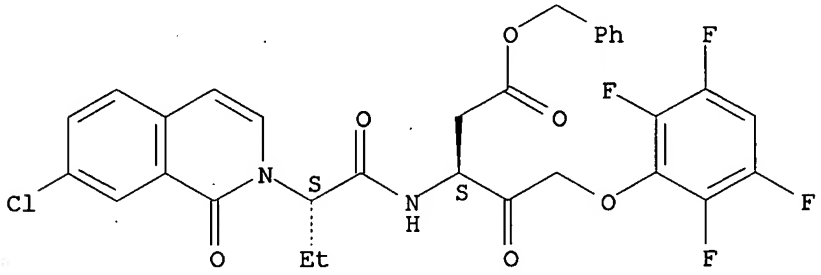
RN 721397-95-1 CAPLUS
CN Pentanoic acid, 3-[[(2S)-2-(7-chloro-1-oxo-2(1H)-isoquinolinyl)-1-oxobutyl]amino]-4-oxo-5-(2,3,5,6-tetrafluorophenoxy)-, 1-methylethyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



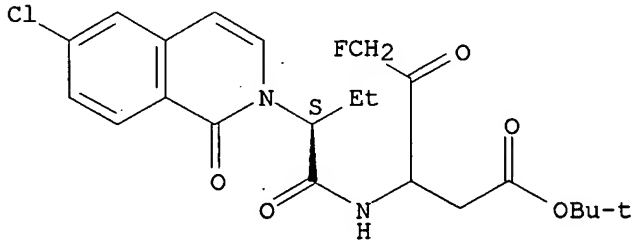
RN 721397-96-2 CAPLUS
CN Pentanoic acid, 3-[[(2S)-2-(7-chloro-1-oxo-2(1H)-isoquinolinyl)-1-oxobutyl]amino]-4-oxo-5-(2,3,5,6-tetrafluorophenoxy)-, phenylmethyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



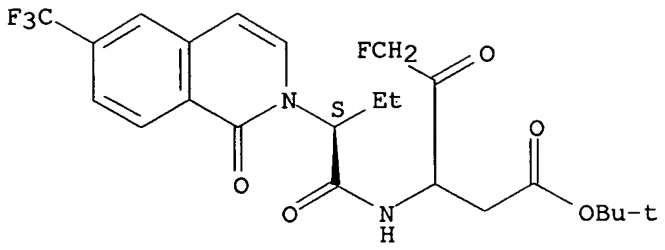
RN 721397-97-3 CAPLUS
CN Pentanoic acid, 3-[[(2S)-2-(6-chloro-1-oxo-2(1H)-isoquinolinyl)-1-oxobutyl]amino]-5-fluoro-4-oxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



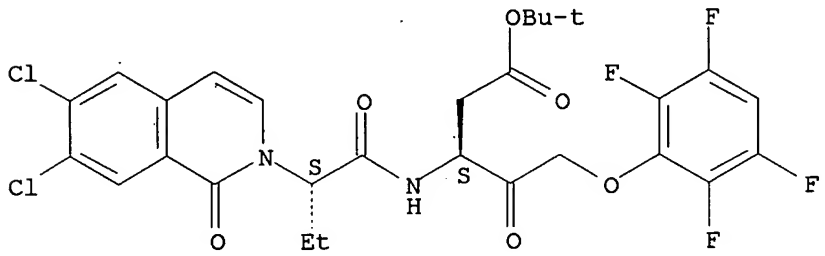
RN 721397-98-4 CAPLUS
CN Pentanoic acid, 5-fluoro-4-oxo-3-[[(2S)-1-oxo-2-[1-oxo-6-(trifluoromethyl)-2(1H)-isoquinolinyl]butyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



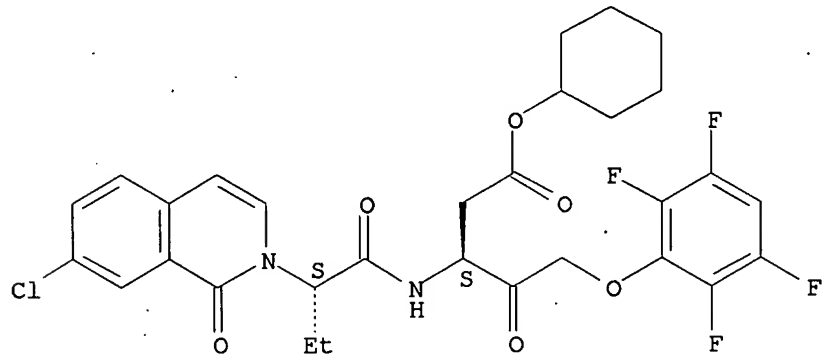
RN 721397-99-5 CAPLUS
CN Pentanoic acid, 3-[[(2S)-2-(6,7-dichloro-1-oxo-2(1H)-isoquinolinyl)-1-oxobutyl]amino]-4-oxo-5-(2,3,5,6-tetrafluorophenoxy)-, 1,1-dimethylethyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



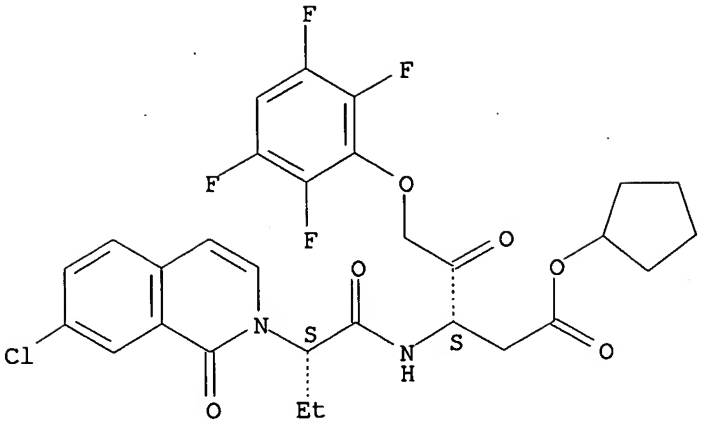
RN 721398-00-1 CAPLUS
CN Pentanoic acid, 3-[[(2S)-2-(7-chloro-1-oxo-2(1H)-isoquinolinyl)-1-oxobutyl]amino]-4-oxo-5-(2,3,5,6-tetrafluorophenoxy)-, cyclohexyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



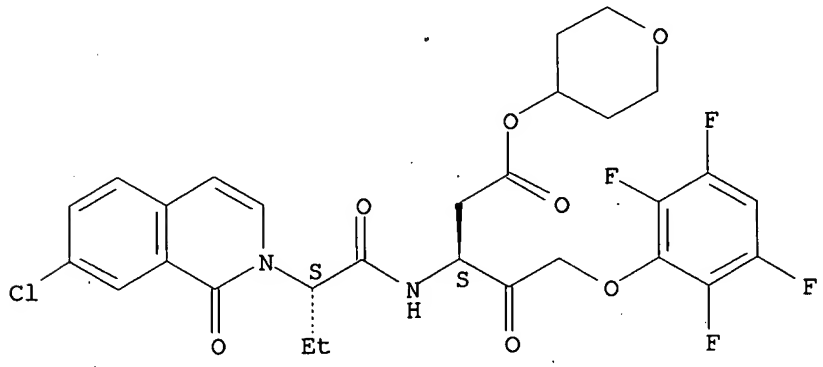
RN 721398-01-2 CAPLUS
CN Pentanoic acid, 3-[[(2S)-2-(7-chloro-1-oxo-2(1H)-isoquinolinyl)-1-oxobutyl]amino]-4-oxo-5-(2,3,5,6-tetrafluorophenoxy)-, cyclopentyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



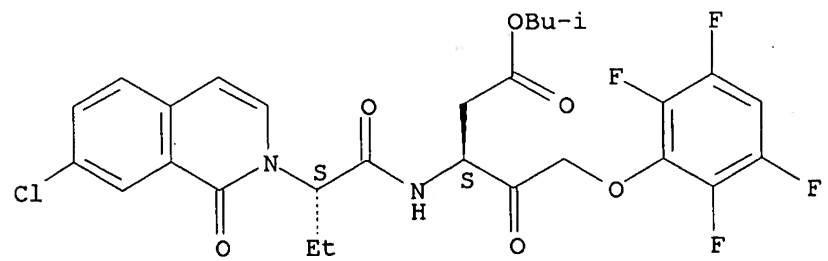
RN 721398-02-3 CAPLUS
CN Pentanoic acid, 3-[[(2S)-2-(7-chloro-1-oxo-2(1H)-isoquinolinyl)-1-oxobutyl]amino]-4-oxo-5-(2,3,5,6-tetrafluorophenoxy)-, tetrahydro-2H-pyran-4-yl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



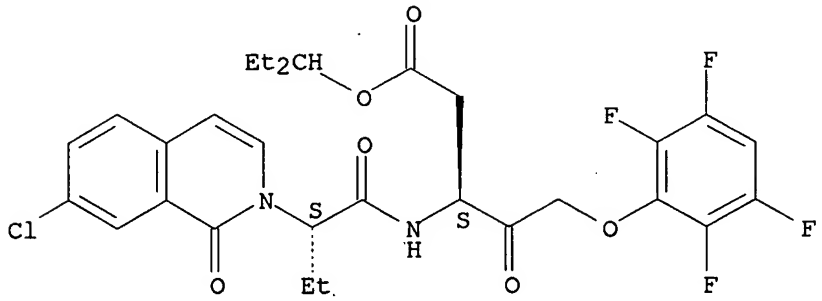
RN 721398-03-4 CAPLUS
CN Pentanoic acid, 3-[[(2S)-2-(7-chloro-1-oxo-2(1H)-isoquinolinyl)-1-oxobutyl]amino]-4-oxo-5-(2,3,5,6-tetrafluorophenoxy)-, 2-methylpropyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



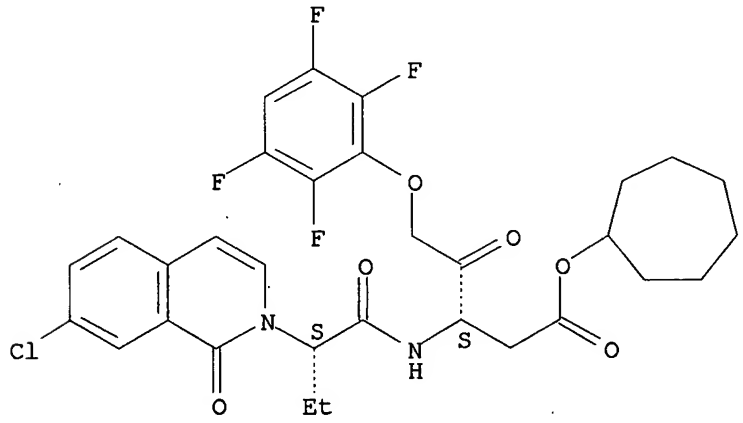
RN 721398-04-5 CAPLUS
CN Pentanoic acid, 3-[[(2S)-2-(7-chloro-1-oxo-2(1H)-isoquinolinyl)-1-oxobutyl]amino]-4-oxo-5-(2,3,5,6-tetrafluorophenoxy)-, 1-ethylpropyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



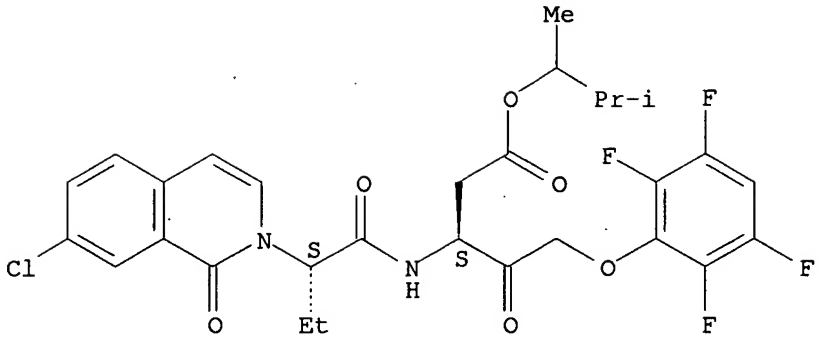
RN 721398-05-6 CAPLUS
CN Pentanoic acid, 3-[[(2S)-2-(7-chloro-1-oxo-2(1H)-isoquinolinyl)-1-oxobutyl]amino]-4-oxo-5-(2,3,5,6-tetrafluorophenoxy)-, cycloheptyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



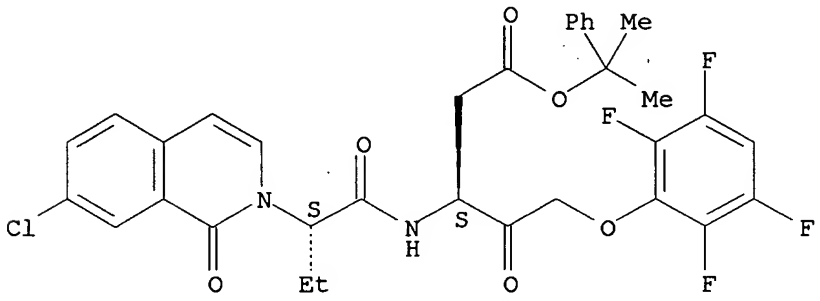
RN 721398-06-7 CAPLUS
CN Pentanoic acid, 3-[[(2S)-2-(7-chloro-1-oxo-2(1H)-isoquinolinyl)-1-oxobutyl]amino]-4-oxo-5-(2,3,5,6-tetrafluorophenoxy)-, 1,2-dimethylpropyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



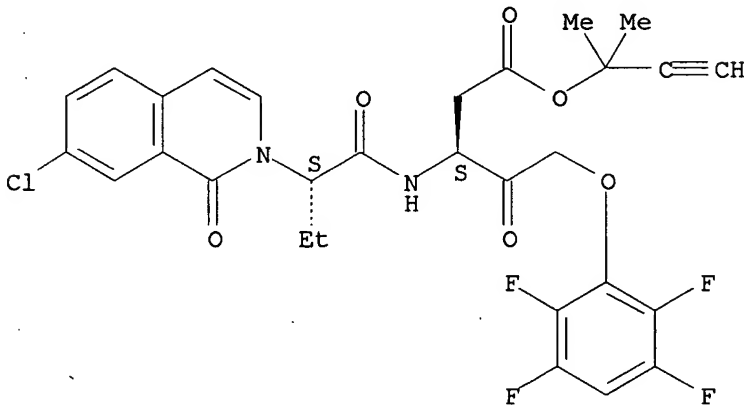
RN 721398-07-8 CAPLUS
CN Pentanoic acid, 3-[[(2S)-2-(7-chloro-1-oxo-2(1H)-isoquinolinyl)-1-oxobutyl]amino]-4-oxo-5-(2,3,5,6-tetrafluorophenoxy)-, 1-methyl-1-phenylethyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 721398-08-9 CAPLUS
CN Pentanoic acid, 3-[[(2S)-2-(7-chloro-1-oxo-2(1H)-isoquinolinyl)-1-oxobutyl]amino]-4-oxo-5-(2,3,5,6-tetrafluorophenoxy)-, 1,1-dimethyl-2-propynyl ester, (3S)- (9CI) (CA INDEX NAME)

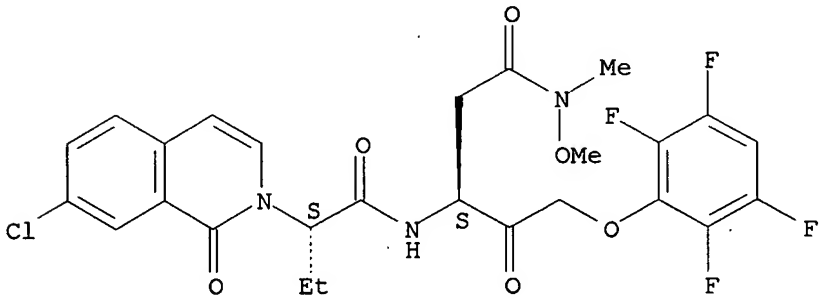
Absolute stereochemistry.



RN 721398-09-0 CAPLUS

CN 2(1H)-Isoquinolineacetamide, 7-chloro-α-ethyl-N-[(1S)-1-[2-(methoxymethylamino)-2-oxoethyl]-2-oxo-3-(2,3,5,6-tetrafluorophenoxy)propyl]-1-oxo-, (αS)- (9CI) (CA INDEX NAME)

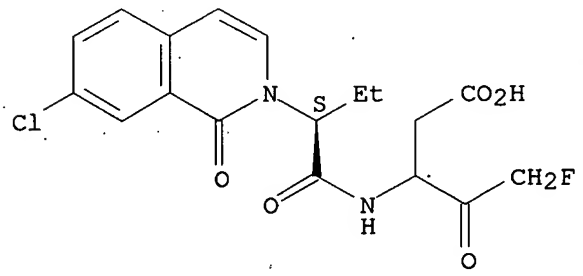
Absolute stereochemistry.



IT **618459-84-0P 640286-42-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of (oxoisoquinolinylacetylamino)-oxopentanoic acid ester and amide derivs. as caspase inhibitors)

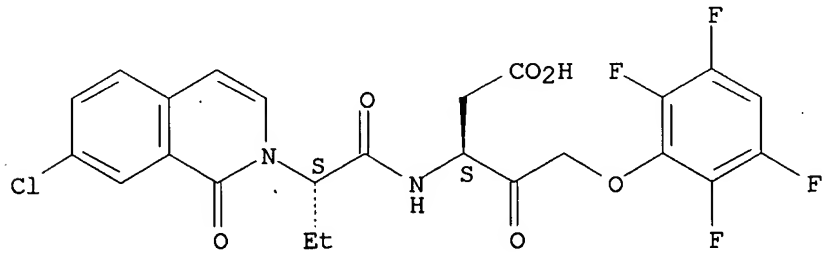
RN 618459-84-0 CAPLUS
CN Pentanoic acid, 3-[[(2S)-2-(7-chloro-1-oxo-2(1H)-isoquinolinyl)-1-oxobutyl]amino]-5-fluoro-4-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 640286-42-6 CAPLUS
CN Pentanoic acid, 3-[[(2S)-2-(7-chloro-1-oxo-2(1H)-isoquinolinyl)-1-oxobutyl]amino]-4-oxo-5-(2,3,5,6-tetrafluorophenoxy)-, (3S)- (9CI) (CA INDEX NAME)

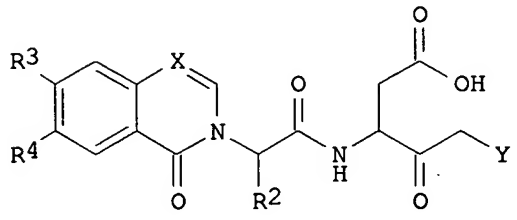
Absolute stereochemistry.



L6 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:20662 CAPLUS
DN 140:77410
TI Preparation of isoquinolinone and quinazolinone peptide derivatives as caspase inhibitors
IN Knegtel, Ronald; Mortimore, Michael; Studley, John; Millan, David
PA Vertex Pharmaceuticals Incorporated, USA
SO PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004002961	A1	20040108	WO 2003-US20557	20030627
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2493646	AA	20040108	CA 2003-2493646	20030627
	US 2004072850	A1	20040415	US 2003-609147	20030627
	BR 2003012232	A	20050510	BR 2003-12232	20030627
	EP 1539701	A1	20050615	EP 2003-762231	20030627
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRAI	US 2002-392592P	P	20020628		
	US 2002-435073P	P	20021220		
	WO 2003-US20557	W	20030627		

OS MARPAT 140:77410
GI



I

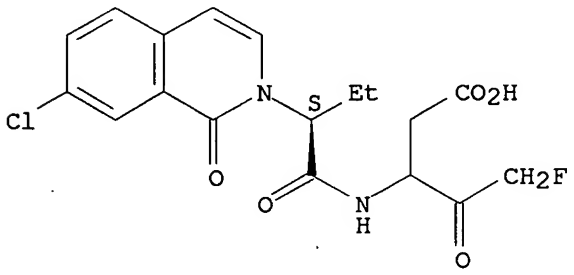
AB The invention relates to isoquinolinones and quinazolinones I [X is CH or N; Y is halo, tri- or tetrafluorophenoxy; R2 is alkyl; R3 is H, halo, OCF3, CN, or CF3; R4 is groups R3 or alkylthio, (un)substituted Ph, phenoxy, or phenylthio; with the proviso that when Y is halo, then R3 and

R4 are not both H] which are caspase inhibitors useful in compns. for the treatment of various diseases, conditions, or disorders. Thus, I (X = CH, Y = F, R2 = Et, R3 = H, R4 = Cl), prepared by coupling of (S)-2-(7-chloro-1-oxo-1H-isoquinolin-2-yl)butyric acid (preparation given) with 3-amino-5-fluoro-4-hydroxypentanoic acid tert-Bu ester, had Ki (M-1 s-1) > 500,000 for inhibition of caspase-1 or caspase-3, Ki 100,000-500,000 for inhibition of caspase-8, and IC50 < 1 μM for inhibition of interleukin-1β secretion.

IT **618459-84-0P 618460-05-2P 618460-11-0P 618460-12-1P 640286-34-6P 640286-35-7P 640286-42-6P 640286-43-7P 640286-48-2P 640286-49-3P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of isoquinolinone and quinazolinone peptide derivs. as caspase inhibitors)

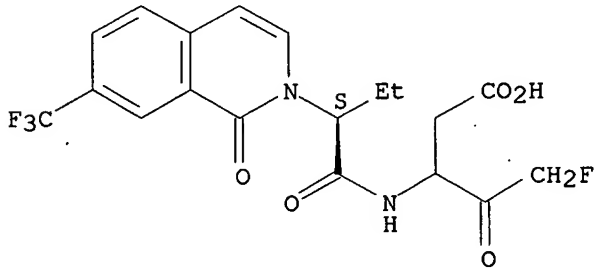
RN 618459-84-0 CAPLUS
CN Pentanoic acid, 3-[[(2S)-2-(7-chloro-1-oxo-2(1H)-isoquinolinyl)-1-oxobutyl]amino]-5-fluoro-4-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



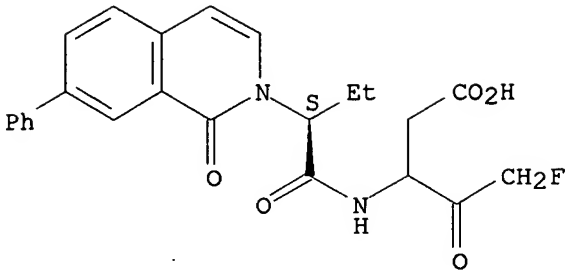
RN 618460-05-2 CAPLUS
CN Pentanoic acid, 5-fluoro-4-oxo-3-[[(2S)-1-oxo-2-[1-oxo-7-(trifluoromethyl)-2(1H)-isoquinolinyl]butyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



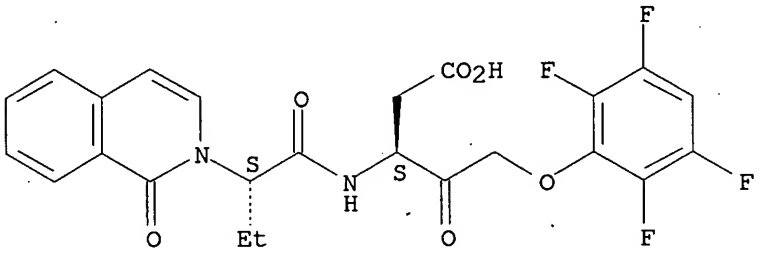
RN 618460-11-0 CAPLUS
CN Pentanoic acid, 5-fluoro-4-oxo-3-[[(2S)-1-oxo-2-(1-oxo-7-phenyl-2(1H)-isoquinolinyl)butyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



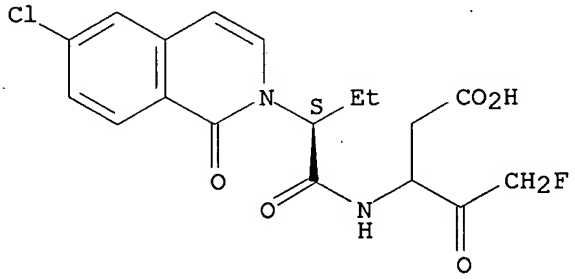
RN 618460-12-1 CAPLUS
CN Pentanoic acid, 4-oxo-3-[[(2S)-1-oxo-2-(1-oxo-2(1H)-isoquinolinyl)butyl]amino]-5-(2,3,5,6-tetrafluorophenoxy)-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



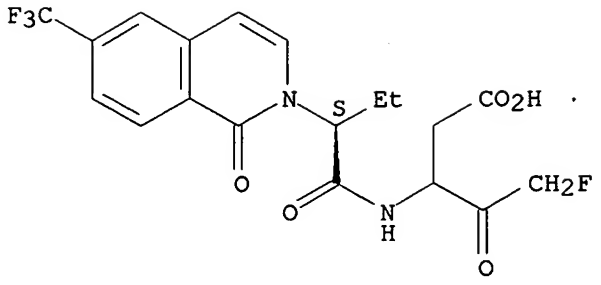
RN 640286-34-6 CAPLUS
CN Pentanoic acid, 3-[[(2S)-2-(6-chloro-1-oxo-2(1H)-isoquinolinyl)-1-oxobutyl]amino]-5-fluoro-4-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



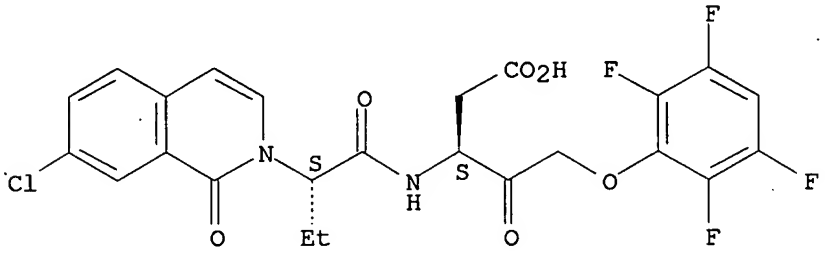
RN 640286-35-7 CAPLUS
CN Pentanoic acid, 5-fluoro-4-oxo-3-[[(2S)-1-oxo-2-[1-oxo-6-(trifluoromethyl)-2(1H)-isoquinolinyl]butyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



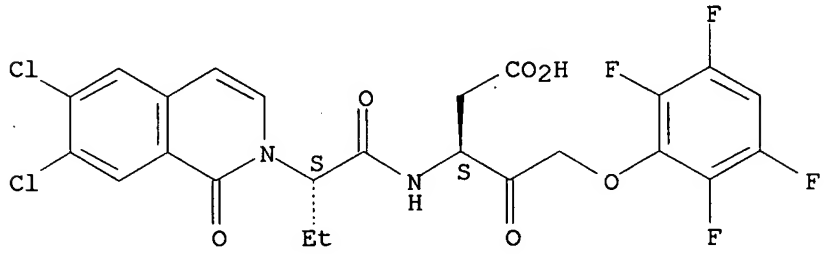
RN 640286-42-6 CAPLUS
CN Pentanoic acid, 3-[[(2S)-2-(7-chloro-1-oxo-2(1H)-isoquinolinyl)-1-oxobutyl]amino]-4-oxo-5-(2,3,5,6-tetrafluorophenoxy)-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



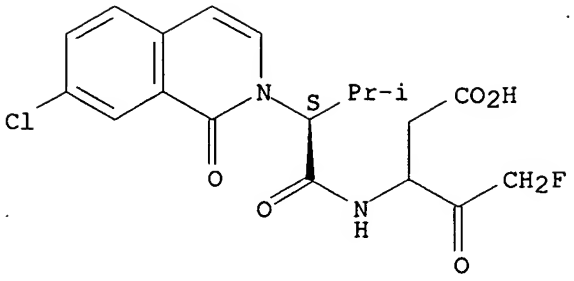
RN 640286-43-7 CAPLUS
CN Pentanoic acid, 3-[[(2S)-2-(6,7-dichloro-1-oxo-2(1H)-isoquinolinyl)-1-oxobutyl]amino]-4-oxo-5-(2,3,5,6-tetrafluorophenoxy)-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



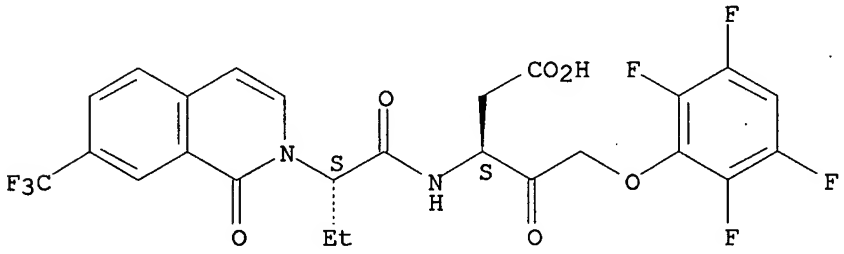
RN 640286-48-2 CAPLUS
CN Pentanoic acid, 3-[[(2S)-2-(7-chloro-1-oxo-2(1H)-isoquinolinyl)-3-methyl-1-oxobutyl]amino]-5-fluoro-4-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



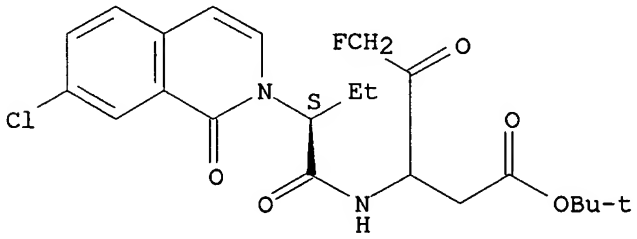
RN 640286-49-3 CAPLUS
CN Pentanoic acid, 4-oxo-3-[[(2S)-1-oxo-2-[1-oxo-7-(trifluoromethyl)-2(1H)-isoquinolinyl]butyl]amino]-5-(2,3,5,6-tetrafluorophenoxy)-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **640286-59-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of isoquinolinone and quinazolinone peptide derivs. as caspase inhibitors)
RN 640286-59-5 CAPLUS
CN Pentanoic acid, 3-[[(2S)-2-(7-chloro-1-oxo-2(1H)-isoquinolinyl)-1-oxobutyl]amino]-5-fluoro-4-oxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



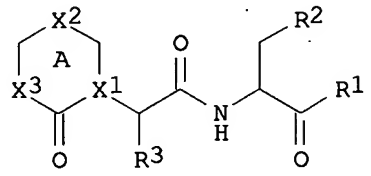
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:991174 CAPLUS

DN 140:28050
TI Synthesis of peptide heterocyclic derivatives as caspase inhibitors
IN Golec, Julian M. C.; Charifson, Paul S.; Charrier, Jean-Damien; Binch, Hayley
PA UK
SO U.S. Pat. Appl. Publ., 28 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003232846	A1	20031218	US 2002-166437	20020610
PRAI US 2002-166437		20020610		

OS MARPAT 140:28050
GI



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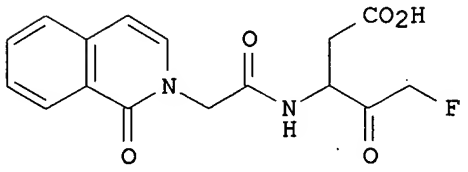


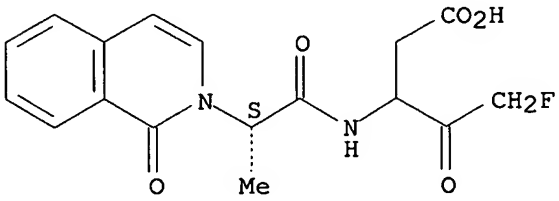
II

AB Compds. I and their synthesis are claimed [R1 = H, CN, CHN2, (substituted)alkyl, aryl, non-aromatic heterocycle, etc.; R2 = CH2COOH, CO2H (or ester/amide/isosteres of); R3 = H or alkyl; X1, X3 = N or C; X2 = bond, O, S, N or C wherein any X with suitable valence may bear a substituent; each C in ring A may also be substituted; ring A substituents = H, halo, alkyl, aryl, OH, CN, etc.; A may also bear a fused ring]. Over 20 synthetic examples are given. Thus, substitution of bromoacetic acid Et ester with the corresponding isoquinolone followed by saponification and coupling to 3-amino-5-fluoro-4-hydroxypentanoic acid tert-Bu ester provided the hydroxy ester intermediate. Oxidation of the hydroxy ester followed by treatment with TFA yielded II as a white powder. Compds. of the invention are caspase inhibitors; data is provided for caspase-1,-3,-7 and caspase-8 inhibition (Ki). Also determined was inhibition of IL-1β secretion from peripheral blood mononuclear cells and activity in a Fas ligand induced apoptosis assay. Compound II had Ki (M-1 s-1) of 248,000 for caspase-1, 130,000 for caspase-3 and an IC50 of 2.9 μM for IL-1β secretion. Compds. I may be used as a component of immunotherapy for the treatment of cancer.

IT **344461-03-6P 344461-10-5P**
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

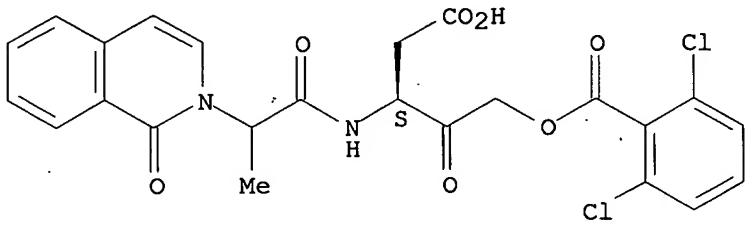
(synthesis of peptide heterocyclic derivs. as caspase inhibitors)
RN 344461-03-6 CAPLUS
CN Pentanoic acid, 5-fluoro-4-oxo-3-[[(2S)-1-oxo-2-(1-oxo-2(1H)-isoquinolinyl)propyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



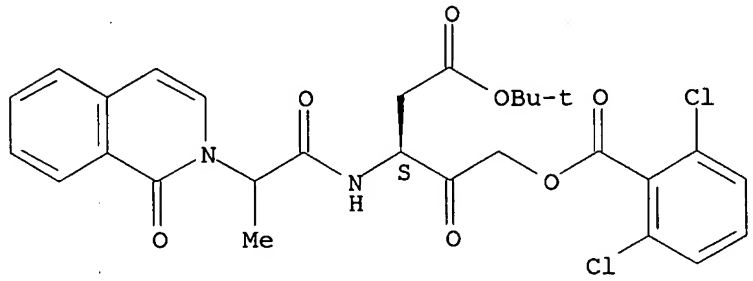
RN 344461-10-5 CAPLUS
CN Benzoic acid, 2,6-dichloro-, (3S)-4-carboxy-2-oxo-3-[[1-oxo-2-(1-oxo-2(1H)-isoquinolinyl)propyl]amino]butyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **344461-30-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of peptide heterocyclic derivs. as caspase inhibitors)
RN 344461-30-9 CAPLUS
CN Benzoic acid, 2,6-dichloro-, (3S)-5-(1,1-dimethylethoxy)-2,5-dioxo-3-[[1-oxo-2-(1-oxo-2(1H)-isoquinolinyl)propyl]amino]pentyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:855766 CAPLUS

DN 139:345913
TI Identification of tumor necrosis factor α (TNF-α) modulator compounds, and use for treatment of TNF-mediated diseases
IN Miller, Karen; Diu-Hercend, Anita; Hercend, Thierry; Lang, Paul; Weber, Peter; Golec, Julian; Mortimore, Michael
PA Vertex Pharmaceuticals Incorporated, USA
SO PCT Int. Appl., 268 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

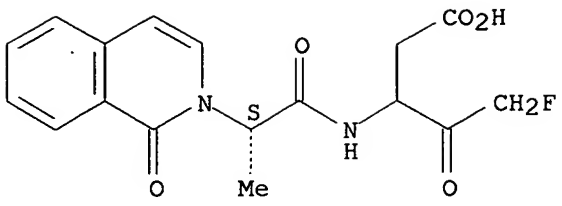
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003088917	A2	20031030	WO 2003-US12262	20030417
	WO 2003088917	A3	20040304		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2004048797	A1	20040311	US 2003-419327	20030417
	EP 1499898	A2	20050126	EP 2003-721795	20030417
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRAI	US 2002-374434P	P	20020419		
	WO 2003-US12262	W	20030417		

AB The invention discloses methods for identifying compds. useful for regulating TNF-α levels and/or activity. The invention also discloses methods for decreasing TNF-α levels and/or activity. Compds. and compns. of the invention are useful for treating TNF-mediated diseases. The invention further discloses kits comprising the compds. and compns. herein and a tool for measuring TNF-α activity and/or levels. Preparation of selected compds., e.g. [3S/R,(2S)]-5-fluoro-4-oxo-3-[(1-(phenothiazine-10-carbonyl)piperidine-2-carbonyl)amino]pentanoic acid, is described.

IT **344461-03-6 344461-10-5 618459-84-0 618459-95-3 618460-05-2 618460-08-5 618460-10-9 618460-11-0 618460-12-1**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(TNF-α modulator compound identification methods, and use for treatment of TNF-mediated diseases)

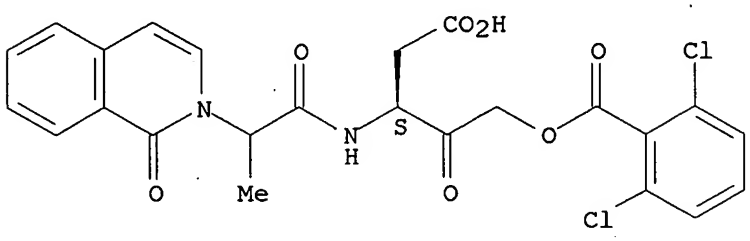
RN 344461-03-6 CAPLUS
CN Pentanoic acid, 5-fluoro-4-oxo-3-[[(2S)-1-oxo-2-(1-oxo-2(1H)-isoquinolinyl)propyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



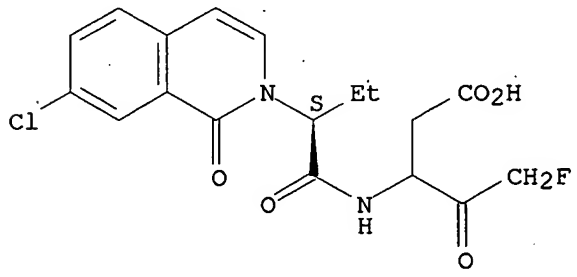
RN 344461-10-5 CAPLUS
CN Benzoic acid, 2,6-dichloro-, (3S)-4-carboxy-2-oxo-3-[[1-oxo-2-(1-oxo-2(1H)-isoquinolinyl)propyl]amino]butyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



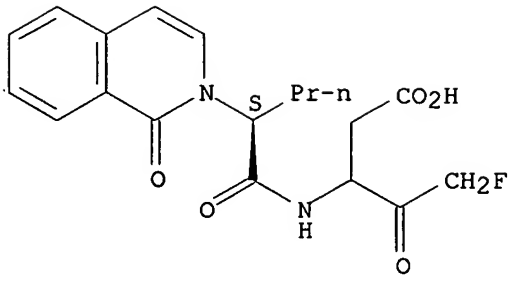
RN 618459-84-0 CAPLUS
CN Pentanoic acid, 3-[[(2S)-2-(7-chloro-1-oxo-2(1H)-isoquinolinyl)-1-oxobutyl]amino]-5-fluoro-4-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



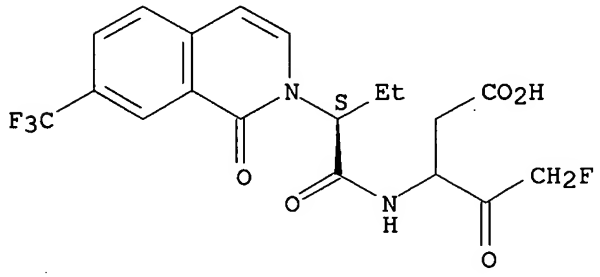
RN 618459-95-3 CAPLUS
CN Pentanoic acid, 5-fluoro-4-oxo-3-[[(2S)-1-oxo-2-(1-oxo-2(1H)-isoquinolinyl)pentyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



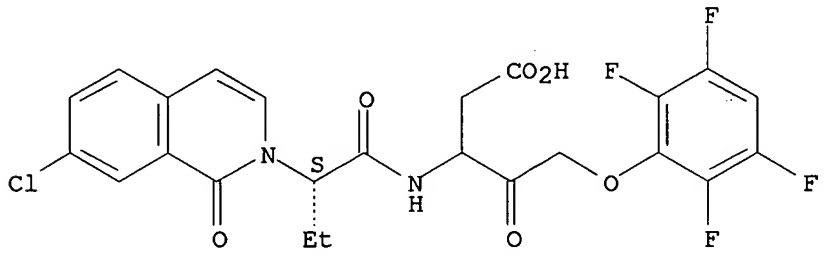
RN 618460-05-2 CAPLUS
CN Pentanoic acid, 5-fluoro-4-oxo-3-[[(2S)-1-oxo-2-[1-oxo-7-(trifluoromethyl)-2(1H)-isoquinolinyl]butyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 618460-08-5 CAPLUS
CN Pentanoic acid, 3-[[(2S)-2-(7-chloro-1-oxo-2(1H)-isoquinolinyl)-1-oxobutyl]amino]-4-oxo-5-(2,3,5,6-tetrafluorophenoxy)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

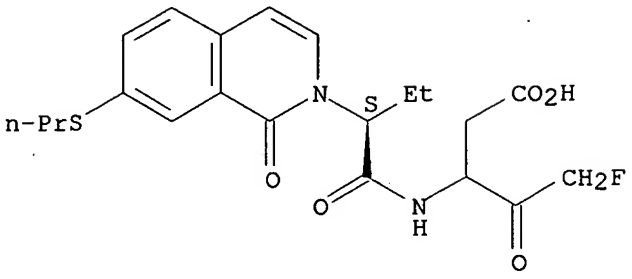


RN 618460-10-9 CAPLUS
CN Pentanoic acid, 5-fluoro-4-oxo-3-[[(2S)-1-oxo-2-[1-oxo-7-(propylthio)-2(1H)-isoquinolinyl]butyl]amino]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

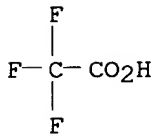
CRN 618460-09-6
CMF C21 H25 F N2 O5 S

Absolute stereochemistry.



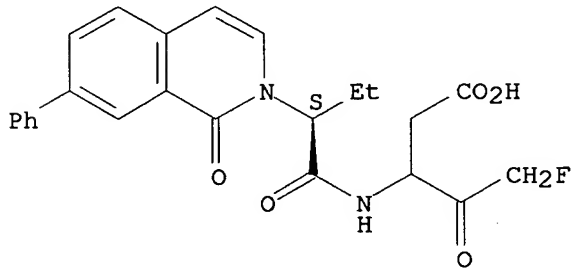
CM 2

CRN 76-05-1
CMF C2 H F3 O2



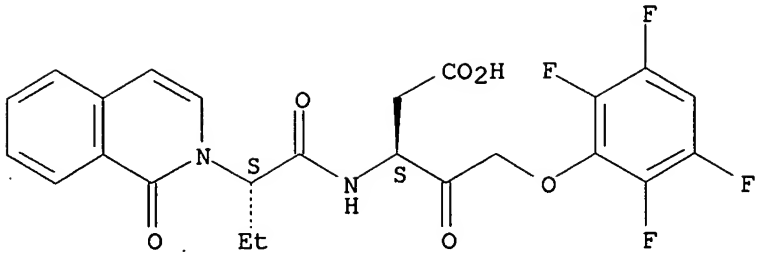
RN 618460-11-0 CAPLUS
CN Pentanoic acid, 5-fluoro-4-oxo-3-[[(2S)-1-oxo-2-(1-oxo-7-phenyl-2(1H)-isoquinolinyl)butyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 618460-12-1 CAPLUS
CN Pentanoic acid, 4-oxo-3-[[(2S)-1-oxo-2-(1-oxo-2(1H)-isoquinolinyl)butyl]amino]-5-(2,3,5,6-tetrafluorophenoxy)-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



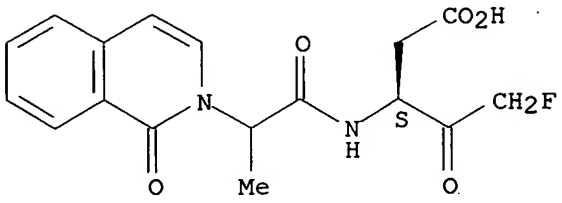
L6 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:656594 CAPLUS
DN 139:191460
TI Phospholipids as caspase inhibitor prodrugs
IN Mortimore, Michael; Golec, Julian M. C.
PA Vertex Pharmaceuticals Incorporated, USA
SO PCT Int. Appl., 256 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003068242	A1	20030821	WO 2003-US4457	20030211
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2004019017	A1	20040129	US 2003-366192	20030211
	EP 1485107	A1	20041215	EP 2003-739810	20030211
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRAI	US 2002-355889P	P	20020211		
	WO 2003-US4457	W	20030211		

OS MARPAT 139:191460
AB The invention relates to compds. which are prodrugs of caspase inhibitors and pharmaceutically acceptable salts thereof. The invention further relates to the release of caspase inhibitors from these compds. through selective bond cleavage. The invention further relates to pharmaceutical compns. comprising these compds., which are particularly well-suited for treatment of caspase-mediated diseases, including inflammatory and degenerative diseases. The invention further relates to methods for preparing compds. of this invention.
IT **582317-55-3**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phospholipids as caspase inhibitor prodrugs)
RN 582317-55-3 CAPLUS
CN Pentanoic acid, 5-fluoro-4-oxo-3-[[1-oxo-2-(1-oxo-2(1H)-

isoquinolinyl)propyl]amino]-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L5 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:435047 CAPLUS
DN 135:46192
TI Synthesis and use of heterocyclic substituted-amido halopentanoate derivatives as caspase inhibitors
IN Golec, Julian; Charifson, Paul; Charrier, Jean-Damien; Binch, Hayley
PA Vertex Pharmaceuticals Incorporated, USA
SO PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001042216	A2	20010614	WO 2000-US33260	20001208 <--
	WO 2001042216	A3	20020228		
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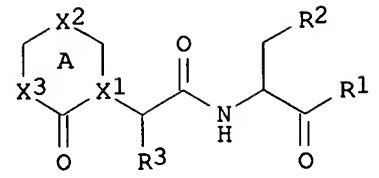
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2393710	AA	20010614	CA 2000-2393710	20001208 <--
	BR 2000016282	A	20020827	BR 2000-16282	20001208 <--
	EP 1244626	A2	20021002	EP 2000-988026	20001208 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2003516393	T2	20030513	JP 2001-543517	20001208
	NZ 519424	A	20040326	NZ 2000-519424	20001208
	ZA 2002004390	A	20030602	ZA 2002-4390	20020531
	NO 2002002656	A	20020806	NO 2002-2656	20020605 <--
PRAI	US 1999-169812P	P	19991208		
	WO 2000-US33260	W	20001208		

OS MARPAT 135:46192
GI



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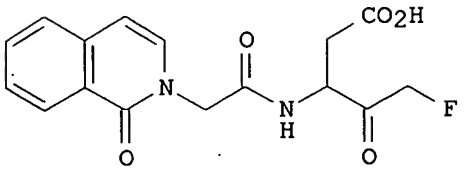

II

AB Compds. I and their synthesis are claimed [wherein; R1 = H, CN, CHN2, (substituted)alkyl, aryl, non-aromatic heterocycle, etc.; R2 = CH2COOH, COOH (or ester/amide/isosteres of); R3 = H or alkyl; X1, X3 = N or C; X2 = bond, O, S, N or C wherein any X with suitable valence may bear a substituent; each C in ring A may also be substituted; ring A substituents = H, halo, alkyl, aryl, OH, CN, etc.; A may also bear a fused ring]. Over 20 synthetic examples are given. For instance; substitution of bromoacetic acid Et ester with the corresponding isoquinolone followed by saponification and coupling to 3-amino-5-fluoro-4-hydroxypentanoic acid tert-Bu ester provided the hydroxy ester intermediate. Oxidation of the hydroxy ester followed by treatment with TFA yielded II as a white powder. Compds. of the invention are caspase inhibitors; data is provided for caspase-1,-3,-7 and caspase-8 inhibition (Ki). Also determined was inhibition of IL-1β secretion from peripheral blood mononuclear cells and activity in a Fas ligand induced apoptosis assay. Compound II had Ki (M-1 s-1) of 248,000 for caspase-1, 130,000 for caspase-3 and an IC50 of 2.9 μM for IL-1β secretion. Compds. I may be used as a component of immunotherapy for the treatment of cancer.

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	30.14	191.68

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-4.38	-4.38

STN INTERNATIONAL LOGOFF AT 12:51:54 ON 08 JUL 2005

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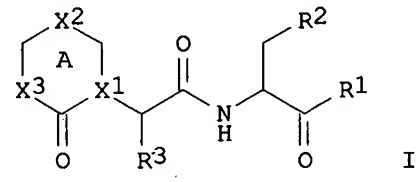
L5 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:435047 CAPLUS
DN 135:46192
TI Synthesis and use of heterocyclic substituted-amido halopentanoate derivatives as caspase inhibitors
IN Golec, Julian; Charifson, Paul; Charrier, Jean-Damien; Binch, Hayley
PA Vertex Pharmaceuticals Incorporated, USA
SO PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001042216	A2	20010614	WO 2000-US33260	20001208 <--
	WO 2001042216	A3	20020228		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2393710	AA	20010614	CA 2000-2393710	20001208 <--
	BR 2000016282	A	20020827	BR 2000-16282	20001208 <--
	EP 1244626	A2	20021002	EP 2000-988026	20001208 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2003516393	T2	20030513	JP 2001-543517	20001208
	NZ 519424	A	20040326	NZ 2000-519424	20001208
	ZA 2002004390	A	20030602	ZA 2002-4390	20020531
	NO 2002002656	A	20020806	NO 2002-2656	20020605 <--
PRAI	US 1999-169812P	P	19991208		
	WO 2000-US33260	W	20001208		

OS MARPAT 135:46192
GI



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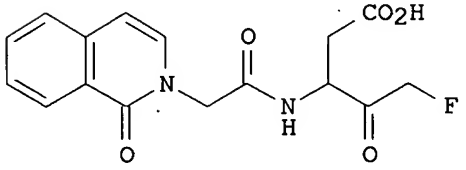


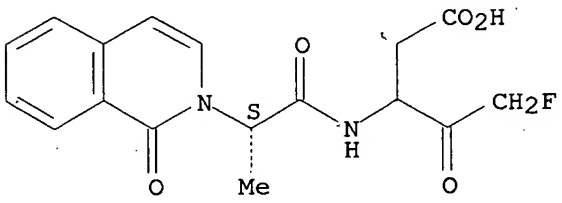
II

AB Compds. I and their synthesis are claimed [wherein; R1 = H, CN, CHN2, (substituted)alkyl, aryl, non-aromatic heterocycle, etc.; R2 = CH2COOH, COOH (or ester/amide/isosteres of); R3 = H or alkyl; X1, X3 = N or C; X2 = bond, O, S, N or C wherein any X with suitable valence may bear a substituent; each C in ring A may also be substituted; ring A substituents = H, halo, alkyl, aryl, OH, CN, etc.; A may also bear a fused ring]. Over 20 synthetic examples are given. For instance; substitution of bromoacetic acid Et ester with the corresponding isoquinolone followed by saponification and coupling to 3-amino-5-fluoro-4-hydroxypentanoic acid tert-Bu ester provided the hydroxy ester intermediate. Oxidation of the hydroxy ester followed by treatment with TFA yielded II as a white powder. Compds. of the invention are caspase inhibitors; data is provided for caspase-1,-3,-7 and caspase-8 inhibition (Ki). Also determined was inhibition of IL-1β secretion from peripheral blood mononuclear cells and activity in a Fas ligand induced apoptosis assay. Compound II had Ki (M-1 s-1) of 248,000 for caspase-1, 130,000 for caspase-3 and an IC50 of 2.9 μM for IL-1β secretion. Compds. I may be used as a component of immunotherapy for the treatment of cancer.

IT **344461-03-6P 344461-10-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and use of heterocyclic substituted-amido halopentanoate derivs. as caspase inhibitors)

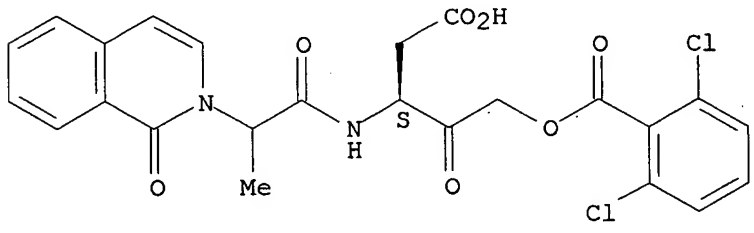
RN 344461-03-6 CAPLUS
CN Pentanoic acid, 5-fluoro-4-oxo-3-[[(2S)-1-oxo-2-(1-oxo-2(1H)-isoquinolinyl)propyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 344461-10-5 CAPLUS
CN Benzoic acid, 2,6-dichloro-, (3S)-4-carboxy-2-oxo-3-[[1-oxo-2-(1-oxo-2(1H)-isoquinolinyl)propyl]amino]butyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



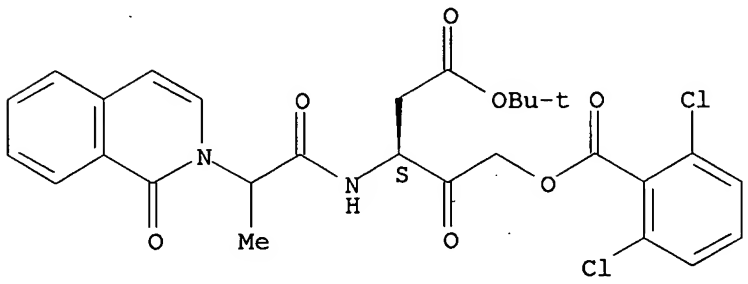
IT **344461-30-9P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and use of heterocyclic substituted-amido halopentanoate derivs. as caspase inhibitors)

RN 344461-30-9 CAPLUS

CN Benzoic acid, 2,6-dichloro-, (3S)-5-(1,1-dimethylethoxy)-2,5-dioxo-3-[[1-oxo-2-(1-oxo-2(1H)-isoquinolinyl)propyl]amino]pentyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	7.28	168.82

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-0.73	-0.73

STN INTERNATIONAL LOGOFF AT 12:57:55 ON 08 JUL 2005